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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,568	01/03/2007	Susan J. Knox	STAN-333	3872

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Stanford University Office of Technology Licensing
Bozicevic, Field & Francis LLP
1900 University Avenue
Suite 200
East Palo Alto, CA 94303

EXAMINER

CHOI, FRANK I

ART UNIT	PAPER NUMBER
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1616

MAIL DATE	DELIVERY MODE
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07/07/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/576,568	Applicant(s) KNOX ET AL.	
	Examiner FRANK I. CHOI	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 April 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6,8-11 and 15-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,6,8-11 and 15-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 April 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The Claims are directed to a method of treating a neoplastic disease in a subject by administering inorganic selenium salt and radiation therapy.

Claims 1-4, 6, 8-11, 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stiefel et al. (US Pat. 6,656,509) in view of the acknowledged prior art, Lemelson et al. (US Pat. 4,665,897) and Gorun (US Pat. 6,511,971).

Stiefel et al. expressly disclose a method for producing a synergistic cytotoxic effect on a cancer cell in a patient being treated for cancer by contact the cell with at least one sale of SeO₂ and a cytostatic agent, where the administration can be simultaneous, separate or sequential, where the cancer is prostatic carcinoma (Claim 1, Claim 6). It is disclosed that a preferred salt of SeO₂ is Na₂SeO₃ (Column 6, lines 1, 2).

The Applicant acknowledges that prostate cancer cells can be resistant to apoptosis which plays a role in local and distant disease progression following conventional therapy, such as radiotherapy (Specification, paragraph 0003). It is acknowledged that selenite is capable of inhibiting cell growth and inducing apoptosis in a variety of human cancer cell lines in vitro, inhibit tumor growth of breast and ovarian cancer cells in vivo, and that the induction of

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apoptosis is mediated by a redox mechanism involving induction of oxidative stress via superoxide formation and lowered intracellular GSH levels (Specification, paragraph 0006).

Lemelson et al. disclose the use of antibodies which target tumor tissue and contain nuclide which can be rendered radioactive by a beam of neutron to generate radiation at the cite of cancerous tissue, such as tumors, thereby destroying the cancerous tissues (Column 10, lines 19-68).

Gorun disclose treatment of tumors with photodynamic sensitizers which produce singlet molecular oxygen and destroys the cancerous tissue (Column 11, lines 14-40).

Stiefel et al. disclose a method for producing a synergistic cytotoxic effect on a cancer cell in a patient being treated for cancer by contact the cell with at least one sale of SeO_2 and a cytostatic agent, where the administration can be simultaneous, separate or sequential, where the cancer is prostatic carcinoma and the preferred salt of SeO_2 is Na_2SeO_3 . The difference between Stiefel et al. and the claimed invention is that Stiefel et al. does not expressly disclose the use of inorganic selenite, radiation therapy or reactive oxygen species (ROS)-inducing therapy. However, the prior art amply suggests the same as Steifel et disclose that sodium selenite is a preferred source of selenium, the applicant acknowledges that radiotherapy is used to treat prostate cancer, Lemelson discloses use of radiation therapy using neutron beams to active nuclides species at the site of the tumor and Gorun discloses that photodynamic sensitizers which produce singlet molecular oxygen are used to destroy cancerous tissue. As such, one of oridnary skill in the art would have expected that the combination of sodium selenite with other methods of treatment of cancers and tumors would be effective in treating cancers and tumors such as prostate cancer.

The Examiner has duly considered the Applicant's arguments but deems them unpersuasive.

The Applicant argues that evidence of synergistic activity has been provided. Said evidence consists of specific amounts of and types of selenite and radiation against two cell lines in vitro and a conclusion that treatment of mice with single cell line tumors, without presenting any data, that the effect was significantly greater than that of radiation or selenite alone. The claims, however, are directed to a method of treating any neoplastic disease in a subject with any type of inorganic selenium compound in any effective amount to alter redox state of tumor cell toward oxidation and type of radiation without limitation as to duration and amount of radiation. As such, the in vitro data is not commensurate in scope with the claims as the claims are not directed to treatment of specific cell lines in vitro with specific amounts of a selenite and a radiation treatment but treatment of any neoplastic disease in a subject with a wide range of amounts of an inorganic selenium compound and types, amounts and duration of radiation treatments. With respect to the mice, no data is provided, as such, the Examiner is unable to determine whether or not the Applicant's conclusions are valid with respect to any synergistic activity. Therefore, the mice evidence in combination with the in vitro data is not sufficient to overcome the *prima facie* conclusion of obviousness.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

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Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a compressed schedule and may be reached Monday, Tuesday, Wednesday and Thursday, 6:00 am – 4:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Johann R. Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frank Choi
Patent Examiner
Technology Center 1600
July 7, 2009

/John Pak/
Primary Examiner, Art Unit 1616